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New Mixed Phosphonate Esters by Transesterification of Pinacol Phosphonates and Their Use in Aldehyde and Ketone Coupling Reactions with Nonstabilized Phosphonates

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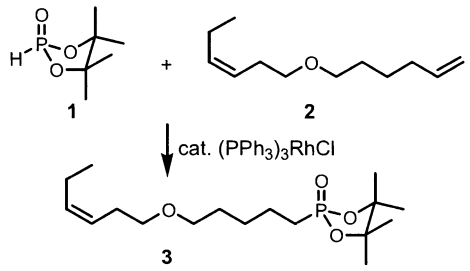
Alkylpinacol phosphonates were prepared by rhodium-catalyzed olefin hydrophosphorylation, and attempted α-deprotonation of the pinacol derived alkyl phosphonates resulted in ring cleavage. The propensity of the alkylpinacol phosphonates to undergo ring opening was exploited to prepare phosphonic acid monomethyl esters in high yield by transesterification in acidulated methanol. Esterification and alkylation with aldehydes or ketones gave *β*-hydroxy mixed phosphonate esters. *tert*-Butyl and benzylic phosphonate ester protective groups were introduced to improve the efficiency and functional group compatibility of *β*-hydroxy phosphonate saponification. The *β*-hydroxy phosphonic acid monomethyl esters were dehydrated with diisopropylcarbodiimide, which gave oxaphosphetane intermediates that collapse to an olefin. The overall reaction sequence complements the arsenal of Horner−Wadsworth−Emmons-type coupling reactions.

Recently, we described a novel method for the utilization of nonstabilized *β*-hydroxy phosphonates in Horner−Wadsworth−Emmons-type coupling reactions by a mild diisopropylcarbodiimide-mediated dehydration.[1] However, an intermediate step requiring phosphonate ester saponification led to decomposition in a number of *β*-aryl and low molecular weight phosphonates. One avenue for avoiding the decomposition during the saponification step would be to utilize more labile phosphonate esters.

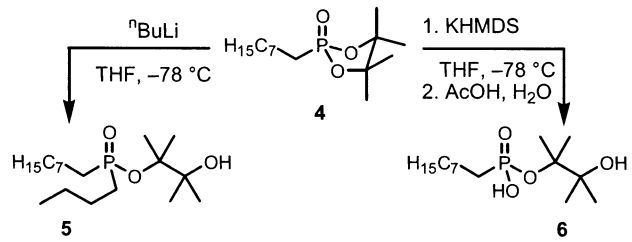
In this regard, we also reported that Wilkinson's complex efficiently catalyzed the hydrophosphorylation of terminal olefins with Tanaka's[2] pinacol hydrogen phosphite **1** (Scheme 1).[3] Under these conditions, the hydrophosphorylation was remarkably selective for a terminal olefin in the presence of other sites of unsaturation. Cyclic phosphonates are generally more reactive and prone to polymerization than their acyclic counterparts,[4] but whether the pinacol phosphonates would prove useful in phosphonate coupling reactions was uncertain given that the chemistry of alkylpinacol phosphonates was virtually unexplored. In this paper, the alkylation and transesterification chemistry of pinacol phosphonates is discussed and a set of orthogonal phosphonate ester protective groups are introduced that extend the scope of the nonstabilized *β*-hydroxy phosphonate olefination reaction.

α-Carbanions of nonactivated phosphonates are readily generated in situ by deprotonation with *n*-BuLi or LDA, and their reaction with aldehydes, ketones, and esters

SCHEME 1



SCHEME 2



is well documented.[5,6] However, ring-cleavage reactions were found to dominate the alkylation chemistry of pinacol phosphonates (Scheme 2), and the attempted deprotonation by treatment with alkyllithiums (e.g., *n*-BuLi, *t*-BuLi, PhLi) or sterically hindered amine bases (e.g., LDA, LiHMDS, NaHMDS, KHMDS, LiTMP) at −78 °C universally resulted in rapid cleavage of the pinacol ester. Evidence for nucleophilic attack at phosphorus by

(1) Reichwein, J. F.; Pagenkopf, B. L. *J. Am. Chem. Soc.*, in press.
(2) Han, L.-B.; Mirzaei, F.; Zhao, C.-Q.; Tanaka, M. *J. Am. Chem. Soc.* **2000**, *122*, 5407−5408.
(3) Reichwein, J. F.; Patel, M. C.; Pagenkopf, B. L. *Org. Lett.* **2001**, *3*, 4303−4306.
(4) Nifant'ev, E. E.; Nasonovskii, I. S.; Miklashevskii, A. V.; Zavalishina, A. I.; Smirnova, E. I. *Zh. Org. Khim.* **1975**, *11*, 2206−2210.
(5) See, e.g.: (a) Collado, I.; Ezquerra, J.; Mazon, A.; Pedregal, C.; Yruretagoyena, B.; Kingston, A. E.; Tomlinson, R.; Wright, R. A.; Johnson, B. G.; Schoepp, D. D. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2849−2854.
(6) Takahashi, H.; Fujiwara, K.; Ohta, M. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1498−1500.

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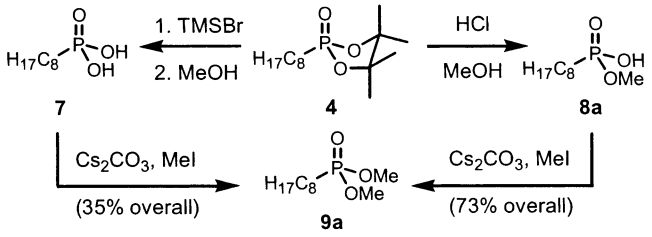
SCHEME 3

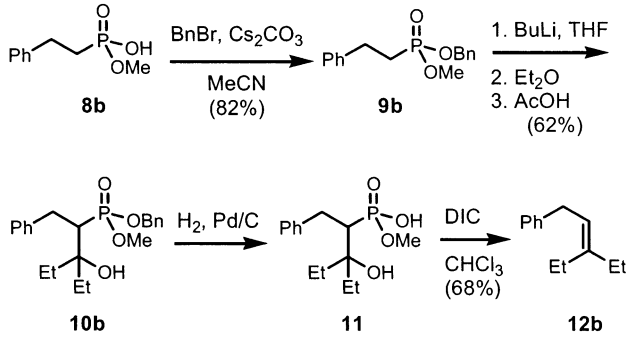


n-BuLi was obtained by isolation of phosphinic ester **5**, and the formation of phosphoramidates was implicated in the reaction with bulky amine bases by the isolation of the phosphonic acid **6** after mild hydrolysis.

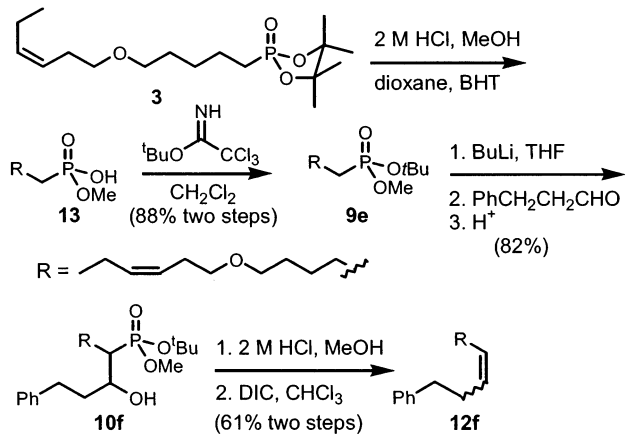
At its current state of development, hydrogen phosphonate **1** unfortunately remains the sole reagent yet identified for transition-metal-catalyzed olefin hydrophosphorylation; therefore, any further progress in the phosphonate alkylation reaction by an α-deprotonation strategy necessitates circumventing reactive intermediate pinacol phosphonates, such as by transesterification to a less reactive phosphonate.[7] Treatment of **4** with Me_3SiBr, which is known to cleave alkyl dimethylphosphonate esters,[8] gave diacid **7** after hydrolysis with dry methanol (Scheme 3). The reaction of **4** with excess HCl in anhydrous methanol hydrolyzed the pinacol ester with greater efficiency, giving the phosphonic acid mono methyl ester **8a**.[9] None of the dimethyl ester **9a** was observed from the transesterification in methanol, but methylation of the crude phosphonic acids **7** and **8a** (Cs_2CO_3, MeI, MeCN) gave the dimethyl octyl phosphonate **9a** in 35% and 75% yield, respectively.[10] Replacing the MeOH in the esterification reaction with ethanol or allyl alcohol was equally effective, but trifluoroethanol resulted in phosphonate decomposition.[11] Curiously, no saponification of phosphonate **4** was observed in NaOH/MeOH.[1] The preparation of dimethyl phosphonate **9a** from the pinacol ester **4** bridges olefin hydrophosphorylation chemistry to the previously established aldehyde and ketone coupling reactions.[1]

In our reported procedure,[1] the strongly basic (2 M NaOH, 16 h) reaction conditions required for the saponification of the dimethyl phosphonate esters caused extensive substrate decomposition in several cases, and it was evident that alternative protective groups were required. A search for complementary phosphonate ester protective groups was greatly simplified by efficient access to phosphonic acid monomethyl esters **8** now possible from the selective transesterification of pinacol phosphonates. Both benzyl and *tert*-butyl esters emerged as the most useful ester protective groups that can be removed under mild conditions yet are compatible with the phosphonate alkylation conditions (Schemes 4 and 5). The monobenzyl phosphonate **9b** was prepared by

SCHEME 4



SCHEME 5



conditions (BnBr, Cs_2CO_3, MeCN, 82%) that were similar to those used to install the methyl ether, and alkylation with 3-pentanone afforded *β*-hydroxy phosphonate **11** in 62% yield. The benzyl ester was removed by hydrogenation (H_2, Pd/C), and without further purification the resulting phosphonic acid was dehydrated with DIC in $CHCl_3$ to give olefin **12b** (68%).

Aldehyde and ketone condensation reactions with the mixed benzyl phosphonate esters are summarized in Table 1. Note that the harsher alkaline conditions required for the saponification of the analogous dimethyl ester **10a** lead to substrate decomposition (Table 1, entry 1). Alkylation of phosphonate **9c** with benzaldehyde (entry 3) provided the benzylic alcohol **10c**, and subsequent deprotection of the benzyl ester (H_2, Pd/C) occurred selectively without over-reduction of the benzylic *β*-alcohol. A slightly reduced yield of 62% was observed with the elimination of adducts from aliphatic aldehydes. The yields for the hydrogenation and elimination steps generally exceed those utilizing the NaOH-mediated saponification, and hydrogenation avoids a difficult aqueous workup altogether.

While hydrogenation is by far the easiest and most common method for removal of a benzyl protecting group, it is usually unsuitable if other sites of unsaturation in the molecule need to remain intact. An alternative protecting group with orthogonal reactivity was desired, and the *tert*-butyl group met this requirement. The olefinic pinacol phosphonate **3** was selected as a model substrate to illustrate the overall coupling sequence and to verify compatibility of the various reactions with a substrate bearing simple functional groups (Scheme 5). Reaction of the phosphonic acid mono methyl ester **13**

(7) See the Supporting Information.

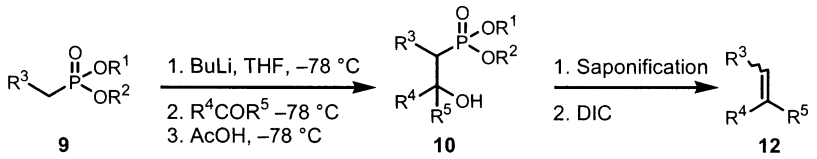
(8) (a) McKenna, C. E.; Higa, M. T.; Cheung, N. H.; McKenna, M.-C. *Tetrahedron Lett.* **1977**, *2*, 155−158. (b) McKenna, C. E.; Schmidhauser, J. *J. Chem. Soc., Chem. Commun.* **1979**, *16*, 739.

(9) See, e.g.: Huber, R.; Knierzinger, A.; Obrecht, J.-P.; Vasella, A. *Helv. Chim. Acta* **1985**, *68*, 1730−1747.

(10) Modification of: Mauger, C.; Masson, S.; Vazeux, M.; Saint-Clair, J.-F.; Midura, W. H.; Drabowicz, J.; Mikolajczyk, M. *Tetrahedron: Asymmetry* **2001**, *12*, 167−174.

(11) A similar observation has been reported by: Fortin, S.; Dupont, F.; Deslongchamps, P. *J. Org. Chem.* **2002**, *67*, 5437−5439.

TABLE 1. Phosphonate Alkylation, Saponification, and Elimination



entry	9	R^1	R^2	R^3	R^4COR^5	yield of 10[a] (%)		saponification[b]	yield of 12[c] (%)	
1	**9a**	Me	Me	C_7H_{15}	Et_2CO	60	**10a**	A or B		**12a**
2	**9b**	Me	Bn	$PhCH_2$	Et_2CO	62	**10b**	C	68	**12b**
3	**9c**	Me	Bn	C_7H_{15}	PhCHO	80	**10c**	C	59	**12c**
4	**9c**	Me	Bn	C_7H_{15}	$PhCH_2CH_2CHO$	57	**10d**	C	55	**12d**
5	**9d**	Me	*t*Bu	$PhCH_2$	$PhCH_2CH_2$ CHO	53	**10e**	D	42	**12e**

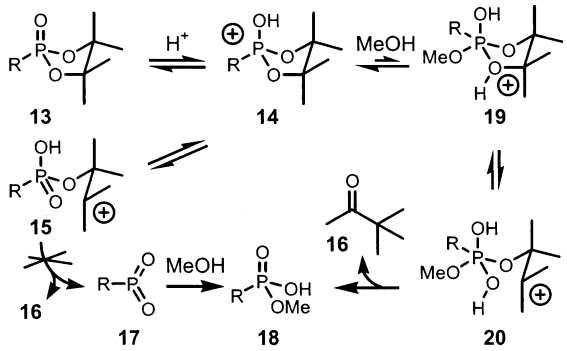
[a] Isolated yields. [b] Saponification methods: A, $MgBr_2$; B, NaOH; C, H_2, Pd/C; D, HCl. [c] Isolated yields for two steps.

with trichloro-*tert*-butyl imidate[12] provided ester **9e** (88%, two steps), and it was interesting to note that the phosphonic acid mono ester was sufficiently acidic to self-catalyze the reaction without additional acid. Alkylation as described above afforded the *β*-hydroxy phosphonate **10f**. Removal of the *tert*-butyl group with HCl in methanol followed by dehydration of the unpurified acid afforded olefin **12f** as a 1:1 mixture of *E* and *Z* stereoisomers in 44% overall yield from **3**. Similar yields were observed with **9d** (Table 1, entry 5).

In some instances, e.g., **3** → **13**, the standard 2 M HCl in MeOH/dioxane combination for cleavage of the pinacol esters surprisingly resulted in extensive decomposition. The mildly acidic conditions used to deprotect the phosphonate ester would not be expected to interfere with unactivated 1,2-disubsituted olefins or aliphatic ethers, and this result (along with several incongruent reactions) suggested a more complicated mode of decomposition was occurring. Addition of the radical scavenger 2,6-di-*tert*-butyl-1-hydroxy toluene (BHT) to the reaction suppressed the decomposition, and to ensure consistent results it is now routinely added to the phosphonate esterification and deprotection reactions described here.

The success of this coupling process was aided by the accessibility of pinacol phosphonates and their unique acid-catalyzed transesterification. Efficient methods for the preparation of phosphonic acid monoprotected esters are desirable as these are useful in the synthesis of biological phosphate analogues,[13] including RNA/DNA,[14] phosphonopeptides,[15] amino acid analogues,[16] pro-drugs,[17] and natural products.[18] A less likely mechanistic hypothesis for the transesterification involves a pinacol-pinacolone rearrangement of the protonated phosphonate **14** followed by collapse to the meta phosphate **17** (Scheme 6),[19] and interception of the reactive meta phosphate

SCHEME 6



intermediate by methanol would give the half-ester **18**. According to this mechanism pinacol cleavage should occur in the absence of methanol, but the phosphonate **14** was stable to both dry HCl in dioxane and triflic acid in CH_2Cl_2. When stoichiometric methanol was added to these reactions at room temperature, less than 20% conversion to **18** occurred after 2 days. The stability of the pinacol phosphonate in the absence of methanol, and the qualitative rate dependence on the methanol concentration suggested a more likely mechanism in which the rate-limiting step will be the formation of phosphorane **19** by reaction with MeOH.[20] Proton-induced pinacol–pinacolone rearrangement will result in the formation of phosphonic acid mono methyl ester **18**. The poor results obtained at low methanol concentration are consistent with the equilibrium lying on the side of pinacol phosphonate **14** instead of pentavalent phosphorane **19**.[21,22]

Conclusion

Benzylic and *tert*-butyl mixed phosphonate esters were introduced to complete a set of orthogonal protective groups for phosphonic acids that further enhances the synthetic utility of olefin hydrophosphorylation and phos-

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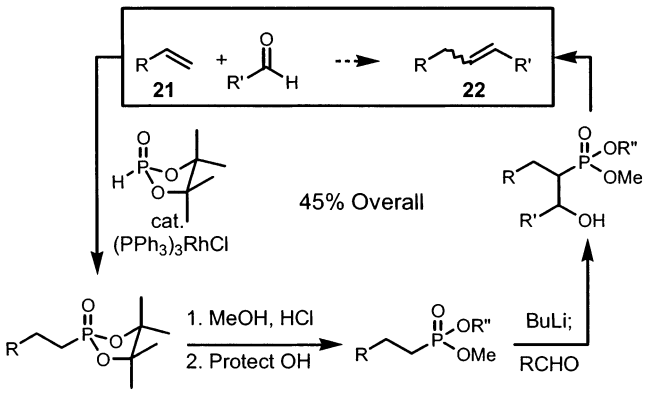
(13) For a review, see: Blackburn, M. G. *Chem. Ind. (London)* **1981**, 134–144.
(14) For a review, see: (a) Eckstein, F.; Thomson, J. B. *Methods Enzymol.* **1995**, *262*, 189–202. (b) Egli, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1894–1909. (c) De Clercq, E. *Biomed. Pharmacother.* **1996**, *50*, 207–215.
(15) For a review, see: Failla, S.; Finocchiaro, P.; Consiglio, G. A. *Heteroatom Chem.* **2000**, *11*, 493–504.
(16) Kafarski P.; Lejczak, B.. *Phosphorus, Sulfur Silicon Relat. Elem.* **1991**, *63*, 193-215.
(17) For a review, see: Krise, J. P.; Stella, V. J. *Adv. Drug. Deliv. Rev.* **1996**, *19*, 287–310.
(18) For a review, see: Fields, S. C. *Tetrahedron* **1999**, *55*, 12237–12273.
(19) Westheimer, F. H. *Chem. Rev.* **1981**, *81*, 313–326.
(20) Perreault, D. M.; Anslyn, E. V. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 432–450.
(21) (a) Ando, K. *J. Org. Chem.* **1999**, *64*, 6815–6821. (b) Brandt, P.; Norrby, P.-O.; Marin, I.; Rein, T. *J. Org. Chem.* **1998**, *63*, 1280–1289.
(22) See also: (a) Motoyoshiya, J.; Kusaura, T.; Kokin, K.; Yokoya, S.-I.; Takaguchi, Y.; Narita, S.; Aoyama, H. *Tetrahedron* **2001**, *57*, 1715–1721. (b) Kluger, R.; Davis, P. P.; Adawadkar, P. D. *J. Am. Chem. Soc.* **1979**, *101*, 5995–6000.

SCHEME 7



phonate coupling reactions with aldehydes and ketones. The overall sequence detailed herein can be routinely executed on multigram scales in ~45% overall yield from starting olefin **21** through to coupled product **22** (Scheme 7). The transesterification of pinacol phosphonates provides a new and efficient method for accessing phosphonic acid mono methyl esters.

Experimental Section[23]

Compounds **3**,[3] and **4**[3] were prepared according to literature procedures. Compounds **8**, **9b**−**e**, **10**, and **12** were prepared by one of the following general methods:

Phosphonic Acid Monomethyl Ester 8a from 4. To a solution of **4** (9.1 mmol) and BHT (3.0 mmol) in MeOH (10 mL) was added 4 M HCl in dioxane (10 mL). The solution was stirred at 50 °C for 3 h and concentrated in vacuo to yield crude **8a**, which was used in the next step without further purification: ^{1}H NMR (CD_3CN, 300 MHz) δ 0.90 (t, J = 6.5 Hz, 3H), 1.30−1.53 (m, 10H), 1.53−1.77 (m, 4H), 3.67 (d, J = 10.8 Hz, 3H); ^{1}H NMR (CD_3OD, 300 MHz) δ 0.92 (t, J = 6.0 Hz, 3H), 1.32−1.42 (m, 10H), 1.56−1.81 (m, 4H), 3.70 (d, J = 10.5 Hz, 3H); ^{13}C NMR (CD_3CN, 75.5 MHz) δ 14.5 (CH_3), 23.5 (CH_2), 23.6 (CH_2), 23.7 (CH_2), 23.9 (CH_2), 25.3 (CH_2), 27.2 (CH_2), 20.2 (CH_2), 31.5 (CH_2), 31.8 (CH_2), 31.9 (CH_2), 33.0 (CH_2), 52.1 (CH_3); ^{13}C NMR (CD_3OD, 75.5 MHz) δ 17.3 (CH_3), 26.3 (CH_2), 26.4 (CH_2), 26.5 (CH_2), 28.1 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 33.1 (CH_2), 34.4 (CH_2), 34.6 (CH_2), 35.8 (CH_2), 55.0 (CH_3), 55.1 (CH_3); ^{31}P NMR (CD_3OD, 121.5 MHz) δ 34.3; ^{31}P NMR (CD_3Cl, 121.5 MHz) δ 38.2; MS (EI) m/z 209 $[M + H]^+$.

Phosphonic Acid Dimethyl Ester 9a from 8a. To a solution of crude **8a** and Cs_2CO_3 (10 mmol) in MeCN (15 mL) was added MeI (26 mmol). The resulting suspension was stirred at 50 °C for 48 h. The reaction mixture was diluted with EtOAc and washed with 10% aqueous HCl (2×), aqueous saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash chromatography gave **9a** as a colorless oil in 73% yield: R_f 0.47 (EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.80 (t, J = 6.6 Hz, 3H), 1.19−1.31 (m, 8H), 1.47−1.72 (m, 4H), 3.66 (d, J = 10.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.2 (CH_3), 22.4 (CH_2), 22.5 (CH_2), 22.8 (CH_2), 23.9 (CH_2), 25.7 (CH_2), 29.2 (CH_2), 30.6 (CH_2), 30.8 (CH_2), 31.9 (CH_2), 52.3 (CH_3), 52.4 (CH_3); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 36.2; MS (EI) m/z 223 $[M + H]^+$; HRMS (EI) calcd for $C_{10}H_{23}O_3P$ $[M + H]^+$ 223.1463, found 223.1462.

Phosphonic Acid Benzyl Ester Methyl Ester 9b from 8b. To a solution of crude **8b** (10 mmol) and Cs_2CO_3 (10 mmol) in MeCN (15 mL) was added BnBr (26 mmol). The resulting suspension was heated at reflux for 48 h, allowed to cool, and then diluted with EtOAc. The organic solution was washed with 10% aqueous HCl (2×), aqueous saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. Purification of the residue by flash chromatography afforded **9b** as a colorless oil in 82% yield: R_f 0.70 (EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.8 Hz, 3H), 1.26−1.36 (m, 10H), 1.54−1.80 (m, 4H), 3.68 (d, J = 10.8 Hz, 3H), 5.09 (d, J = 8.4 Hz, 2H), 7.28−7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.3 (CH_3), 22.5 (CH_2), 22.6 (CH_2), 22.9 (CH_2), 24.7 (CH_2), 26.6 (CH_2), 29.2 (CH_2), 30.7 (CH_2), 30.9 (CH_2), 32.1 (CH_2), 52.3 (CH_3), 67.3 (CH_2), 67.4 (CH_2), 128.1 (CH), 128.6 (CH), 128.8 (CH), 136.8 (C), 136.9 (C); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 35.7; MS (CI) m/z 299 $[M + H]^+$; HRMS (CI) calcd for $C_{16}H_{27}O_3P$ $[M + H]^+$ 299.1776, found 299.1773.

***β*-Hydroxy Phosphonates 10a from 9a.** To a cooled (−78 °C) solution of **9a** (0.80 mmol) in THF (2.5 mL) was added *n*-BuLi in hexanes (0.80 mmol). After the mixture was stirred at −78 °C for 15 min, the aldehyde (0.80 mmol) in THF (1 mL) was added. After 60 min at −78 °C, aqueous NH_4Cl was added to the cold mixture. After being warmed to room temperature, the mixture was extracted with EtOAc, and the organic layer was washed with brine and dried ($MgSO_4$). Purification by flash chromatography afforded **10a** as a colorless oil in 60% yield: R_f 0.65 (EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.80−0.87 (m, 9H), 1.15−1.68 (m, 16 H), 1.97−2.09 (m, 1H), 3.65−3.73 (m, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 7.5 (CH_3), 7.6 (CH_3), 14.2 (CH_3), 22.8 (CH_2), 26.5 (CH_2), 28.6 (CH_2), 28.7 (CH_2), 29.2 (CH_2), 30.0 (CH_2), 30.5 (CH_2), 30.6 (CH_2), 32.0 (CH_2), 43.6 (CH), 52.2 (CH_3), 52.3 (CH_3), 52.4 (CH_3), 75.3 (C); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 39.1; MS (CI) m/z 309 $[M + H]^+$, 291 $[M - H_2O + H]^+$.

Olefins 12b from 10b. A solution of **10b** (1.1 mmol) in EtOH (5 mL) containing a catalytic amount of Pd/C was shaken at room temperature for 16 h under an H_2 atmosphere (250 psi), and the resulting mixture was concentrated in vacuo to afford crude **11**. Without further purification, **11** was dissolved in $CHCl_3$ (5 mL) and DIC (2.2 mmol) was added. After being stirred at room temperature for 4 h, the reaction mixture was concentrated in vacuo, and the residue was purified by flash chromatography to give **12b** as a colorless oil in 68% yield: R_f 0.73 (hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (t, J = 7.5 Hz, 6H), 2.18 (q, J = 7.5 Hz, 2H), 2.26 (q, J = 7.5 Hz, 2H), 3.48 (d, J = 7.2 Hz, 2H), 5.39 (t, J = 7.2 Hz, 2H), 7.25−7.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.8 (CH_3), 13.2 (CH_3), 23.3 (CH_2), 29.2 (CH_2), 33.8 (CH_2), 121.1 (CH), 125.7 (CH), 128.3 (CH × 2), 141.9 (C), 143.8 (C).

Phosphonic Acid *tert*-Butyl Ester Methyl Ester 9d from 8b. To a solution of crude **8b** (4.3 mmol) in CH_2Cl_2 (10 mL) and cyclohexane (10 mL) was added *tert*-butyl 2,2,2-trichloroimidate (43 mmol) portionwise. The resulting slurry was stirred for 16 h and then concentrated in vacuo. Purification of the residue by flash chromatography afforded **9d** as a colorless oil in 62% yield: R_f 0.30 (EtOAc/hexane 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.52 (s, 9H), 1.98−2.10 (m, 2H), 2.87−2.95 (m, 2H), 3.71 (d, J = 11.1 Hz, 3H), 7.23−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.69 (d, J = 143 Hz, CH_2), 28.72 (d, J = 4.4 Hz, CH_2), 30.24 (d, J = 3.9 Hz, CH_3), 51.79 (d, J = 6.6 Hz, CH_3), 82.26 (d, J = 9.4 Hz, C), 126.1 (CH), 127.9 (CH), 128.4 (CH), 141.02 (d, J = 17.6 Hz, C); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 39.1; MS (CI) m/z 401 $[M + H]^+$; HRMS (CI) calcd for $C_{13}H_{21}O_3P$ $[M + H]^+$ 257.1307, found 257.1317.

Olefins 12e from 10e. To a solution of **10e** (0.68 mmol) in MeOH (2.5 mL) was added 4 M HCl in dioxane (2.5 mL). The reaction mixture was stirred for 2 h and then concentrated in vacuo. The residue was dissolved in $CHCl_3$, and DIC (1.36 mmol) was added. The reaction mixture was stirred for 2 d and then concentrated in vacuo. Purification of the residue by flash chromatography afforded **12e** as a colorless oil in 42% yield: R_f 0.31 (hexane/EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.42−2.49 (m, 1H), 2.55−2.62 (m, 1H), 2.77−2.84 (m, 2H), 3.42 (t, J = 5.1 Hz, 2H), 5.64−5.69 (m, 2H), 7.18−7.41 (m, 10H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 29.6 (CH_2), 33.8 (CH_2), 34.7

(23) For general experimental details, see: Reichwein, J. F.; Iacono, S. T.; Pagenkopf, B. L. *Tetrahedron* **2002**, *58*, 3813−3822.

(CH_2), 36.2 (CH_2), 39.3 (CH_2), 126.1 (CH), 126.2 (CH), 128.6 (CH), 128.7 (CH), 128.8 (CH), 129.2 (CH), 129.9 (CH), 130.0 (CH), 131.3 (CH), 141.3 (C), 142.2 (C), 142.3 (C).

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Supporting Information Available: Preparation and characterization data for **5**−**10** and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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